

**AMENDMENTS TO THE SPECIFICATION****In the Specification:**

Please replace the second paragraph at page 43 with the following replacement paragraph:

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, CREMOPHOR ~~Cremophor~~ EL™ (BASF, Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition will be sterile and should be fluid to the extent that easy syringability exists. A composition will be stable under the conditions of manufacture and storage and are preferably preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Please replace the first paragraph at page 48 with the following replacement paragraph:

The NOD mouse model for diabetes was used in these examples. The NOD mouse undergoes an autoimmune destruction of pancreatic islet B cells similar to that seen in patients with human type I diabetes. Infiltration of CD4+ and CD8+ T cells into the Islets of Langerhans

begins at 4-5 weeks of age. These Examples show that, in contrast to whole anti-CD28 antibody PV1 (also referred to herein as PV1.10.17, as described in U.S. Patent No. 5,948,893), PV1-scFv surprisingly prevents disease onset in both weanling NOD as well as adult female NOD mice.

Please replace the second paragraph at page 48 with the following replacement paragraph:

Example 1. Anti-CD28 (PV1) and ~~PV1 (anti-CD28)-scFv~~ PV1-scFv bind to CD28 equally.

BIAcore experiments have been done comparing the binding of PV1, PV1-scFV, mCD28.Fc (murine CD28 fused to IgG Fc domain) and mIgG2A (murine IgG2A) to murine CD28 (mCD28.Fc), which show that PV1-scFv and anti-CD28 (PV1.10.17) bind equally well to murine CD28 (Figure 1).

Please replace the third paragraph at page 48 with the following replacement paragraph:

Example 2. PV1-scFv ~~PV1 (anti-CD28)-scFv~~ inhibits T cell responses *in vitro*.

PV1-scFv blocks costimulation of anti-CD3 responses *in vitro* (Figure 2). In this example,  $1 \times 10^5$  NOD spleen cells were cultured with 1  $\mu\text{g/ml}$  anti-CD3. PV1-scFv or mCTLA4-Ig were added on day 0. Proliferation (cpm of  $^3\text{H}$ -thymidine incorporated into the DNA of the cells) was measured on day 3.

Please replace the fourth paragraph at page 48 with the following replacement paragraph:

Example 3. PV1-scFv ~~PV1 (anti-CD28)~~ delays disease onset in two week old NOD female mice.

Two to three week old female NOD mice were injected with 50 $\mu\text{g}$  PV1-scFv every other day for two weeks with an additional dose at five, six, and seven weeks. At 27 weeks of age, only 20% of the PV1-scFv treated mice were diabetic, in contrast, 80% of control mice were diabetic (Figure 3). In this example, 50  $\mu\text{g}$  PV1-scFv or 710-Fab, was administered to 2 week old female NOD mice every other day for 14 days with an additional dose at 5, 6, and 7 weeks.

Please replace the fifth paragraph at page 48 with the following replacement paragraph:

Example 4. PV1-scFv delays disease onset in adult (8 week old) NOD female mice.

Adult female NOD mice were injected with 50  $\mu$ g PV1-scFv daily from eight to ten weeks. At thirty weeks of age, only 40% of the PV1-scFv treated mice were diabetic, in contrast, 100% of control mice were diabetic (Figure 4). In this example, 8 week old female NOD mice were injected with 50  $\mu$ g of PV1-scFv or control antibody daily for 14 days.